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Prevalence and treatment of neurological and psychiatric disorders among tertiary hospitals in Pakistan; findings and implications

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Abstract

Introduction: Mental health and neurological disorders are prevalent in Pakistan. However, there are considerable concerns with their management due to issues of access, availability of trained personnel and stigma alongside paucity of such data. Consequently, there is a need to document current treatment approaches starting with tertiary hospitals in Pakistan where patients with more severe mental and neurological disorders are typically treated. Subsequently, use the findings to help direct future policies and initiatives. **Methods:** Multi-centred, cross-sectional, prospective study principally evaluating current medicine usage among patients attending tertiary hospitals in Pakistan with psychiatric and neurological disorders. In addition, possible factors contributing to the prevalence of these disorders in this population to help with future care. All 23 tertiary care hospitals in the ten major Districts in Pakistan were included, which cover 75% of the population. **Results:** 57664 patients were evaluated of which 35.3% were females. Both females and males had multiple brain disorders and multiple co-morbidities. Schizophrenia was the most prevalent disorder overall among both females (25.2%) and males (30.4%). A median of six medicines were prescribed per patient, with antipsychotics and antidepressants the most prescribed medicines. Clozapine was the most prescribed medicine in males (12.25%) and females (11.83%) including for psychiatric disorders, with

sodium valproate the most prescribed medicine in epilepsy in males (42.44% of all anti-epileptic medicines) as well as females (46.38%). There was a greater prevalence of both disorders among the lower classes. A greater prevalence of schizophrenia was seen in patients abusing alcohol and smokers. The divorce rate was higher among the studied patients and the prevalence of depression was higher among the widowed population. **Conclusions:** There were concerns with the quality of prescribing including the extent of polypharmacy as well as possible overuse of clozapine especially in patients with epilepsy, both of which need addressing.

1. INTRODUCTION

1.1 Mental health issues across countries LMICs and in Pakistan

Mental health disorders currently account for between 10 to 13% of the global burden of diseases, although others have documented higher rates (1-7). The global burden of these disorders has risen in recent years, especially among lower- and middle-income countries (LMICs), as a result of demographic, environmental and socio-political changes (8-10). However, there are challenges as there is currently limited government spending on mental disorders across LMICs as well as typically only a limited number of professionals available in LMICs to treat patients with mental health conditions (3, 4, 10-12). Typically in LMICs, mental health services are lacking, and large segments of the population do not have ready access to mental health service professionals and/ or receive inadequate care (7, 13-16).

In Pakistan, mental problems currently affect between 10–16% of the population or greater (17, 18), most of whom are women. These high rates in Pakistan are exacerbated by increasing unemployment rates, insecurity, political fluctuations, disruption of social norms and a high percentage of the population living below the poverty level (19-21). However, the provision of mental health services is a challenge in Pakistan especially regarding important issues such as access to appropriate care (18, 21). There are currently no specific community based residential facilities or community based out-patient treatment facilities for patients with psychiatric disorders in Pakistan. , This is not helped by the fact that the majority of the Pakistani population are unwilling to accept people having mental health problems, which results in active discrimination towards those with psychiatric disorders in the country (21).

Typically care for patients with psychiatric disorders is provided in hospitals in Pakistan, which include both tertiary care hospitals as well as secondary care hospitals in the large cities, with patients living in both rural and urban areas typically visiting these facilities for their care. Overall, there are 1280 tertiary care hospitals in Pakistan. However, access to care and medicines as well as misplaced beliefs may lead patients to seek help from local religious healers and practitioners of traditional medicines rather than healthcare professionals, which can result in very limited relief (21). Women in Pakistan face an even greater risk of psychiatric disorders with challenges accessing services as well as being subject to domestic violence (21). Encouragingly though, more patients with psychiatric disorders are now accessing professionals in Pakistan as a result of the growing awareness of these disorders and the ability of healthcare professionals to treat these (21). Having said this, there are continuing concerns with the training of physicians in Pakistan regarding the treatment of patients with psychiatric disorders, which is similar to many other LMICs (5, 10),

1.3 Neurological diseases in LMICs including Pakistan

Neurological diseases are also a concern, and does include psychiatric disorder co-morbidities (22). This is certainly the case among patients referred to tertiary hospitals in Pakistan for their treatment. In their 2006 report, the WHO estimated that by 2030, 80% of all strokes will occur in LMICs (23). As economies improve in LMICs, with associated changes in lifestyle, diet and the environment, the prevalence of diseases more often associated with Western countries will increase. This has been the case with for instance high rates of cardiovascular diseases now found among LMICs including sub-Saharan African countries with changes in diet and lifestyles (24-27).

In Pakistan, there was a 13.5% increase in the prevalence of neurological disorders in all age groups as well as disability-adjusted life-years (DALYs) from 1990 to 2015, and a 18.5% decrease in age standardised rates in the same period (28). Epilepsy is seen as the second most burdensome neurological condition worldwide (29). Current prevalence rates in Pakistan are 10 per 1000 persons, with people living in urban areas nearly twice as likely to have epilepsy compared with those living in rural areas (30). Females are also more likely to have epilepsy (10.9 per 1000 persons) than males

(9.2 per 1000 persons) (30). The rate of strokes is also rising in Pakistan similar to other LMICs with growing rates of cardiovascular disease (31, 32), with an estimated annual incidence of 250 per 100,000 of the population, which translates into approximately 350,000 new cases of stroke every year in Pakistan (33). Currently, one in four people in Pakistan has either hypertension, type-2 diabetes or cardiovascular disease (34, 35), increasing the burden of stroke in the future unless adequately addressed.

We would like to build on these studies to help with the future care of patients with psychiatric and neurological diseases in Pakistan given the current paucity of publications documenting this. There is also a need to document current medicines prescribed to act as a basis for developing pertinent treatment guidelines for patients with these conditions in Pakistan given current concerns with the training of physicians in Pakistan to treat patients with psychiatric disorders. In addition, identifying possible triggers to the development of psychiatric and neurological disorders to help with future prevention strategies. Pertinent quality improvement programmes can also be proposed starting with the most severe patients based on a situational analysis of current treatments. This is similar to the philosophy behind point prevalence studies for antimicrobials in Pakistan and across countries (36-39).

We are aware that studies have been conducted in other countries documenting treatment patterns in patients with neurological and psychiatric disorders, and are just starting in Pakistan including cross national surveys (21, 40-42). However, we believe it is important to conduct such studies in Pakistan as Pakistan is currently the sixth most populous country of the world with an estimated population of 207.77 million in 2017 (43). There are also concerns with the stigma associated with psychiatric disorders in Pakistan, access to care especially in patients with multiple co-morbidities and appropriate prescribing given the paucity of national standard treatment guidelines (STGs) in Pakistan and limited physician training (5, 10, 44). Additional concerns include issues with inappropriate polypharmacy in patients with multiple co-morbidities enhanced by the lack of STGs and physician training. Addressing identified concerns should help improve the future management of patients with both psychiatric and neurological disorders in Pakistan especially given the paucity of such data in Pakistan. The findings may well be of interest to other LMICs struggling to optimally treat patients with psychiatric and neurological disorders.

1.4 Aims of the study

The aims of the study are to document current prevalence proportions, co-morbidities, treatments including issues of polypharmacy, and possible factors in the management of patients with neurological and psychiatric disorders attending tertiary hospitals in Pakistan. By starting with the more severe cases, we believe our findings will help inform physicians and policy makers regarding key issues including current drug utilisation patterns. As a result, help improve the future care of such patients in the Islamic Republic of Pakistan. The lessons learnt in the more severe cases can be used generally to help improve the care of such patients throughout Pakistan with most patients with psychiatric disorders currently treated in secondary and tertiary care facilities in Pakistan.

2. MATERIALS AND METHODS

2.1 Overview of the study

A multi-centred, cross-sectional, prospective drug utilisation study was designed to principally document current medicines prescribed and prevalence proportions for patients with various neurological and psychiatric disorders attending tertiary hospitals across the Islamic Republic of Pakistan. This includes patients with joint co-morbidities. In addition, possible factors influencing the development of these disorders.

We focused on ten major districts among three of the four provinces in Pakistan to give a good representation of Pakistan. We did not add Baluchistan due to law and order concerns in this province. The ten major Districts included Karachi, Hyderabad and Mirpur Khas (Sindh), Peshawar and Abbottabad (Khyber Pakhtunkhawa), Lahore, Faisalabad, Multan, Sargodha and Gujranwala (Punjab), which represent 75% of the Pakistani population, and included all 23 tertiary care hospitals providing such care out of a total of 1280 tertiary care hospitals throughout Pakistan.

Data was collected from tertiary care hospitals, since, as mentioned, this is where patients with neurological and mental health disorders are typically treated in Pakistan when not seeking care from local religious healers or practitioners of traditional medicines.

Data were collected between April 2016 to March 2018. We included all tertiary care hospitals providing care for such patients in this initial comprehensive study as we did not wish to undertake a selection of possible cases as we felt this might bias any findings. Consequently, no statistical analysis was undertaken to determine possible patient numbers for further analysis.

2.2 Inclusion and exclusion criteria

All outpatients and inpatients presenting to the tertiary hospitals during the study period with psychiatric and/or neurological disorders were included in the study. There was no gender discrimination and no random selection of patients. However, patients were broken down where pertinent into males and females given issues of domestic violence and also females currently live longer than males in Pakistan (67.4 years versus 65.7 years for males (45)).

However, patients were excluded if they were pregnant, were unconscious or in a coma, had malignancy or HIV or were disabled. This was in order to focus on the primary conditions and any associated co-morbidities, any ongoing pharmacologic treatment and any potential underlying factors. We were aware based on our experiences that the psychiatric condition among pregnant patients in Pakistan may well change following the delivery of their child. Consequently, we excluded pregnant mothers from our study. The patients who died during the study period were also removed from the study. Past medical history, alcohol and drug abuse, smoking habits, and social status were also considered with alcohol and drug misuse, as well as smoking, related to neurological and psychiatric conditions (46, 47).

The various neurological and psychiatric disorders were evaluated based on ICD-10 (48) and included: Attention Deficit Hyperactivity Disorder (ADHD), Central Auditory Processing Disorder (CAPD), Cerebral Atrophy, Cerebral Palsy, Cluster Headache, Dementia, Drug dependence disorders such as alcohol dependence disorder, Epilepsy, Insomnia, Mentally retardation, Migraine, Parkinson's disease, Parkinsonism and Psychiatric disorders including Attention Deficit Hyperactivity Disorder, Alzheimer's Disease, Bipolar Affective Disorder (BAD), Body Dysmorphic Disorder, Depression, Generalized Anxiety Disorder, Hypomania, Mania, Mood Disorder, Obsessive-Compulsive Disorder (OCD), Paranoia, Phobia, Postpartum Depression, Psychosis, Post-Traumatic Stress Disorder (PTSD) and Schizophrenia. Excluded conditions included sexual dysfunctions, personality disorders, dissociative disorders, somatoform disorders, neuralgia, and demyelinating disorder. The diagnosis was taken from the patient's notes and in discussions with patients with no additional follow-up of physicians. We have included both schizophrenia and psychosis. This is because schizophrenia is a mental illness that causes psychosis; however, schizophrenia also has other symptoms and it is not the only cause of psychosis. Other mental illnesses that cause psychosis including depression, bipolar disorders, dementia and borderline personality disorder. Psychosis may also occur during times of extreme stress, lack of sleep, or trauma. Psychosis may also be caused by a brain injury, neurological problems, or other health problems. Consequently, while psychosis can be a part of schizophrenia, it can be caused by many other factors as well.

2.3 Questionnaire design and collection of survey data

A patient history proforma was designed based on Neurology Questionnaire of Physician's Clinic of Iowa, USA (49) and piloted prior to the study. The survey team were subsequently trained in the use of the standardised questionnaire before initiating the study. After obtaining informed consent, the questionnaire was administered face-to-face in settings that provided maximum privacy by trained personnel, with the questions asked in English, Urdu or a regional language depending upon the patient's capabilities. If the patient answered in Urdu or a regional language, this was converted to English acknowledging that some concepts may not be the same across languages (50). However, concerns were minimised by using trained researchers fluent in the pertinent languages.

The standardised questionnaire included demographic data (age, gender, and address), dietary habits, tobacco and alcohol consumption (46, 47), medical history, socioeconomic status based on income, family history, symptoms of neurological conditions including chronic headaches and, seizures, as well as current medications for psychiatric and neurological disorders. Medicines were classified according to their chemical (INN) name (51). No attempt was made to classify medicines as

an originator, branded generic or generic, as this was not the main aim of this paper. We further assessed medicine use in the four most prevalent conditions to add further insight into current treatment modalities among this patient population, which was a descriptive assessment.

We are aware that many factors that combine together to affect the health of individuals and communities. The determinants of health include social, economic, and physical environments as well as people's individual characteristics and behaviours (52). We are also aware that marital relationship is also an important component of family and social support, and failure to reach or maintain a marriage can go against social norms and expectations in a number of countries including Pakistan, which may influence the extent of especially psychological conditions (53-55). Consequently, we considered the income status, family history including patients' stress conditions, and marital status of patients in our study. We also included family history because conditions including ADHD, Alzheimer's disease, epilepsy, Parkinson's Disease and OCD may run in families (56). We also looked further at smoking habits (57, 58), alcoholic intake (46, 47), and drug misusers (47, 59), in view of their potential impact on neurological and psychiatric disorders.

We defined low-income as patients earning up to US$200 per month; middle-income between US$200 and US$750 per month, and greater than US$750 per month as high-income in line with salaries of personnel in the government and private sectors. Patients' ages were also broken down into 10 age bands in line with other studies, i.e. 0 – 9 years, 10 –19 years, 20 – 29 years, 30 – 39 years, 40 – 49 years, 50 – 59 years, 60 – 69 years, 70 – 79 years, 80 – 89 and above (60, 61).

2.4 Statistical Analysis

Anonymised responses were subsequently entered onto an Excel spreadsheet for analysis. Descriptive statistics and crude prevalence proportions were calculated for the different neurological and psychiatric conditions for patients attending the tertiary hospitals in the various districts of Pakistan during the study period.

Crude prevalence proportions were calculated by dividing the total number of cases during the course of the study by the total number of people attending the tertiary hospitals in the ten major districts among three of the four provinces in Pakistan for these various disorders and adjusting for one year.

Univariate linear regression was used to evaluate the changes. When dealing with age groups, interquartile range (IQR) was identified and applied. All the analyses were undertaken in SPSS version 22 (IBM Corporation USA). No other statistical tests were undertaken as this paper was principally a situational analysis rather than testing any pre-defined hypotheses.

2.5 Ethical considerations

Ethical approval for the study was obtained from the Institutional Ethical Committee of Rashid Latif College of Pharmacy, Lahore. Written informed consent was obtained before enrolling participants into the study.

3. RESULTS

3.1 Patient demographics

Overall 57,664 patients met the inclusion criteria, of which 35.32% were females with a median age (IQR) of 40 (5 to 91) years and 64.68% were males with a median age of 47.5 (5-91 inter quartile range). Most patients were also lower economic status (Table 1).

Insert Table 1

3.2 Distribution of neurological and psychiatric disorders according to age and gender among the study participants

Figure 1 documents the prevalence of the various neurological and psychiatric disorders among the studied patients.

Insert Figure 1

Both females and males had multiple brain disorders as shown in Table 2. Schizophrenia was the most prevalent disorder among both males and females. Males had the lowest prevalence of ADHD

and Parkinson's Disease among those with these formal diagnoses whilst females had the least prevalence of PTSD and post partum depression (Table 2).

Insert Table 2

Patients with epilepsy were typically younger with a median age of 27 (IQR 5 to 70) years versus those with other disorders (Appendix A1). Among patients with neurological disorders, the median age for schizophrenia, psychosis and bipolar affective disorders (BAD) was 31, 32 and 35 years respectively.

Schizophrenia, depression, and epilepsy were among the highest prevalence diagnoses in the study group with Parkinson's disease, postpartum depression, PTSD and ADHD the least common disorders (Table 3). It was found that schizophrenia was most prevalent disorder in males (30.4%) as well as females (25.2%) followed by depression 10.8% and 20.0% respectively (Table 3). Overall, there were low prevalence rates for CAPD, cerebral palsy, hypomania, postpartum depression, PTSD and ADHD (Table 3).

Insert Table 3

57,644 patients were prescribed 207,488 medicines (total number of medicines*),* with a median of six medicines per patient, with antipsychotics and antidepressants the most prescribed medicines in both males and females (Table 4). Of these, 77.29% (n=160368) were psychotropics for schizophrenia and depression with a median of two medicines per patient (Table 5). Clozapine was the most prescribed medicine in males (12.25%) and females (11.83%), with trifluoperazine (0.02, 0.02%), ziprasidone (0.02, 0.02%), oxazepam (0.02, 0.01%), and duloxetine (0.02, 0.0%) the least prescribed in females and males with clofazimine (0.01%) also the least prescribed in males (p = 0.000).

Insert Table 4

The most frequently prescribed medicine among females and males in all age groups with schizophrenia was clozapine (22.17 and 22.27% of all medicines prescribed for schizophrenia) (Table 5), with promethazine the least prescribed antipsychotic for schizophrenia in males (9.08%) and olanzapine the least prescribed in females. Clozapine was also the most prescribed medicine for patients with depression potentially reflecting multiple psychiatric disorders in the studied population. However, sodium valproate was the most prescribed medicine in epilepsy in males (42.44% of all anti-epileptic medicines) as well as females (46.38%), while carbamazepine was least prescribed medicine in males (19.59%) and mirtazapine the least in females (17.47%). Details of patients' co-morbidities are included in the Appendix.

Insert Table 5

The most frequently diagnosed disorder in smokers was schizophrenia in males (30.63%) and females (23.53%). Schizophrenia was also prevalent in patients abusing alcohol (36.36%). Male drug misusers (31.32%) also had schizophrenia, which was mostly followed by depression (13.65%) (Table 6).

Insert Table 6

3.3 Potential causes of neurological and psychiatric Disorders

We further studied family history to ascertain possible factors which could affect the prevalence of psychiatric and neurological disorders in our patient population (Table 7).

Insert Table 7

We found that patients suffering from neurological and psychiatric problems had more fluctuations in their marital affairs (Table 1). Of the 57,664 subject participants in the present study, 22,864 were single. The marriage rate among the subjects of our study was 58.46% compared to 63.04% for the National marital rate according to Pakistan Bureau of Statistics (43). The divorce rate among the studied population was 1.10%, which is more than double the 0.34% rate among the general population (43). It was also observed that the prevalence of depression was high in both male

(5.55%) and female (50%) widowed populations in our study, whilst there was a high rate of schizophrenia in single and married women (26.99%, 25.44% respectively) and men (30.37%, 30.25% respectively).

4. DISCUSSION

We believe this is the most comprehensive study undertaken to date among patients with neurological and psychiatric conditions attending tertiary hospitals in Pakistan to guide future management and policy decisions Both males and females had multiple brain disorders and co-morbidities (Table 2, Appendix B). Overall, schizophrenia, depression, and epilepsy were among the most prevalent diseases within the study group (Table 3), with Parkinson's disease, postpartum depression, PTSD and ADHD the least common (Table 3). This was reflected in the high use of antipsychotics and antidepressants among this population, accounting for a total of 62.9% to 64.1% of all medicines prescribed in females and males respectively (Table 4).

Among those with neurological disorders, the median age for schizophrenia, psychosis and Bipolar affective disorders (BAD) was 31, 32 and 35 years respectively. Other studies have also suggested age and gender differences in the onset of schizophrenia (62, 63). This may be due to differences in diagnostic rates, life styles and living conditions between the patients in the various studies.

There was an appreciable number of medicines prescribed for the patients in our study (Table 4). The high rate of polypharmacy is a concern with a median of six medicines per patient. This may reflect the extensive co-morbidities in the studied patients similar to other studies assessing rates of polypharmacy among patients in Asia including Pakistan with appreciable psychiatric disorders (40, 41). However, this will need closer monitoring as polypharmacy is known to increase the rate of adverse drug reactions with associated increases in hospitalisations, morbidity and mortality as well as negatively impact on adherence rates to the medicines prescribed (64-68). There are a number of initiatives that can subsequently be undertaken to reduce rates of inappropriate prescribing, and we will be looking at these in the future (66, 69-71).

Clozapine was the most frequently prescribed medicine overall (Table 4) as well as in patients with schizophrenia and depression (Table 5), and the second most prescribed medicine in patients with epilepsy (Table 5). This is a concern in patients with depression and epilepsy and will be looked at further; however, this may reflect bias from self-reported illness which may actually represent complex psychiatric co-morbidities or schizoaffective and bipolar disorders rather than solely depression or principally epilepsy (72, 73). This was the same for both sexes, with the high use of clozapine similar to other studies of patients with schizophrenia (74), especially those with more severe disease (21, 75-77), with trifluoperazine, ziprasidone, oxazepam, and duloxetine, the least prescribed in females and males with clofazimine the least prescribed in males (Table 4).

There were also concerns that 12% of patients prescribed a psychotropic medicine were also co-prescribed a benzodiazepine, which is not good clinical practice. However, this is similar to other studies involving patients with severe psychiatric problems in Pakistan (41). It is unclear though if the benzodiazepines were prescribed as acute rescue medicines or for chronic long-term use. Even so, benzodiazepines are known to worsen cognitive impairment (78), depressive symptoms (79, 80), and reduce the effectiveness of some psychological therapies (81) as well as being associated with increased mortality for people with schizophrenia (82). Consequently, their prescribing needs to be carefully considered as part of future management strategies in patients with appreciable co-morbidities, and will be researched further. This can be part of the development of STGs in these patients alongside regular medication reviews and improved physician education regarding mental health disorders. This though requires key physicians from pertinent tertiary hospitals to come together to develop and refine treatment guidelines for their patients in Pakistan with psychiatric and neurological disorders. A starting point could be pertinent international guidelines; however, adapted for the local situation. This important activity could be under the direction of the College of Physicians in Pakistan. Locally produced guidelines with trusted physicians appear to have good adherence in practice as seen for instance in Sweden with its guidance and list of prescribed medicines (83, 84). Such activities, including addressing high rates of polypharmacy, could also be part of any national action plan for patients with mental and neurological disorders in Pakistan, building on WHO and national initiatives across countries (7, 10, 85-87).

There was also limited prescribing of promethazine similar to other studies (21, 88). Harrison and others have concluded that early recognition of treatment resistance schizophrenia and the use of clozapine appears to be associated with reduced hospitalisation (89, 90), supporting its use among patients with schizophrenia in these tertiary centres in Pakistan (Tables 4 and 5). Consequently, it is difficult to fully comment on the appropriateness of clozapine prescribing, which can again be part of any future quality initiatives.

However, our findings are different to Mahmood et al where olanzapine and risperidone were the most prescribed antipsychotics with more limited prescribing of clozapine. This is because their study was conducted in more general (secondary) hospitals compared to just tertiary hospitals (21). Our study population with high rates of co-morbidities (Appendix B) is reflected in the high use of clozapine and sodium valproate in patients with depression (Table 6) reflecting a greater prevalence of bipolar disorders especially bipolar depression. Sodium valproate is prescribed for maintenance treatments in patients with bipolar disorders in view of its effectiveness and tolerability compared with other treatments (91, 92). Sodium valproate was also the most prescribed medicine in male patients with epilepsy as well as in females, whilst carbamazepine was the least prescribed in males and mirtazapine the least in females (Table 5). The appreciable use of clozapine and antidepressants in patients with epilepsy reflects, as mentioned, extensive co-morbidities (Appendix B) similar to other studies (93). Overall, the medicine utilisation patterns seen in our study is different from conventional treatments in ambulatory care due to the large number of co-morbidities (Appendix B) and the availability of medicines in the hospital formulary.

The most frequently diagnosed disorder in smokers was schizophrenia in both males and females (Table 6). This is perhaps not surprising with several studies showing that patients with schizophrenia have an extremely high prevalence of smoking, almost 90%, compared to only 33% in the general population and 45–70% in patients with other psychiatric diagnoses (94-96). Rates of smoking though are now much lower in the general population in developed countries following several campaigns (97, 98). Government campaigns may also start to reduce smoking rates in Pakistan similar to other countries, enhanced by the banning of smoking in public places (99, 100). Schizophrenia was also prevalent in alcoholics (Table 6) (101-103) and male drug misusers (104, 105), followed by depression (Table 6) which have a known association (104, 105).

Family history appeared to have an influence on the prevalence of psychiatric and neurological disorders in our patient population (Table 7). Multiple studies have also revealed that socioeconomic status is a major cause in the progression of neurological and psychiatric disorders (106-109). The prevalence of depression was high in both male and female widowed populations in our study, whilst there was a high rate of schizophrenia in single and married women and men. Several studies have also shown an association between marital status and psychiatric disorders (110, 111).

We are aware there are a number of limitations with our study. These include the fact that we concentrated only on tertiary hospitals in Pakistan without including secondary care hospitals with more generalised populations for the reasons given. We also only assessed prescribing practices at one point in time rather than longitudinally, and we did not assess the rationale behind prescribing practices. We also relied on the responses from patients for a number of social, economic and other factors, although we are aware that it can be very difficult in Pakistan to interview patients with psychiatric disorder as they can be non-responsive especially those from rural areas. However, despite these limitations, we believe our findings are robust given their extensive nature providing a background to the development of suitable initiatives to improve the future care of these patients in Pakistan.

In conclusion, there is a high prevalence of neurological and psychiatric disorders in LMICs such as Pakistan. We have identified a number of factors and issues that we believe increase their prevalence. There are also extensive co-morbidities leading to multiple medicines being prescribed which can be inappropriate as well as concerns with the prescribing of clozapine and benzodiazepines in some patients. These concerns will be researched further given the known association between polypharmacy and medicine adherence rates as well as potential adverse effects, and we will be reporting on this in due course.

Key Points

- There are considerable co-morbidities among patients with mental health and neurological disorders being treated at tertiary hospital in Pakistan
- These co-morbidities lead to polypharmacy among patients with a median of six medicines per patient, with high use of clozapine among the patient groups.
- There are concerns with some of the drug combinations prescribed which needs addressing to reduce morbidity and mortality alongside reviewing the need for an appreciable number of medicines in some patients
- There is also need to standardise management approaches for patients with mental health and neurological disorders among the tertiary hospitals in Pakistan given a lack of standardised treatment guidance to date. Once undertaken, prescribing can be assessed against agreed guidance to improve future care

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CONFLICT OF INTEREST
Authors declare they have no conflicts of interest.

Data availability
Data is available on request.

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Tables

Table 1 – Patient demographics

Population Demographics		
Age (Years)	**Females**	**Males**
	n (%)	**n (%)**
0-9	160 (0.8)	96 (0.3)
10-19	2080 (10.3)	5328 (14.3)
20-29	5776 (28.5)	13712 (36.7)
30-39	5712 (28.2)	9888 (26.5)
40-49	2688 (13.3)	5392 (14.4)
50-59	1984 (9.8)	1584 (4.2)
60-69	1152 (5.7)	976 (2.6)
70-79	624 (3.1)	272 (0.7)
80-89	64 (0.3)	80 (0.2)
90-99	16 (0.1)	16 (0.0)
Economic status	**n (12752)**	**n (21456)**
Lower Income (Class)	12496* (97.99)	14976 (69.80)
Middle Income (Class)	240 (1.88)	5712 (26.62)
Upper Income (Class)	16 (0.12)	768 (3.58)
*11056 are house wives.		
Marital Status		
Single	5216	17648
Married	14304	19408
Separated	96	2
Divorced	448	192
Widowed	288	16

NB: 11056 patients were housewives without income with a number of patients also dependent on others for their income including parents

Table 2 - Distribution of neurological and psychiatric disorders among study participants in order of prevalence

Disorder	Female (n=19095)	Male (n=34965)
Schizophrenia	5136	11328
Depression	4064	4032
Epilepsy	2656	3920
GAD	1328	3536
OCD	1328	3024
Mood Disorder	1168	2784
BAD	1088	1408
Psychosis	976	1248
Mania	848	2064
Dementia	512	944
Phobia	272	608
Insomnia	240	464
Cluster Headache	192	288
Migraine	144	80
AD	96	128
BDD	64	144
Cerebral Atrophy	64	144
MR	64	16
DDD	32	848
PD	32	176
CAPD	16	32
Cerebral Palsy	16	0
Postpartum Depression	16	0
PTSD	16	0
Hypomania	0	32
Paranoia	0	16
Parkinson's Disease	0	16
ADHD	0	16

NB: ADHD (Attention deficit hyperactivity disorder), AD (Alzheimer's disease), BAD (Bipolar affective disorder), BDD (Body dysmorphic disorder), CAPD (Central auditory processing disorder), DDD (Drug dependence disorder), GAD (Generalized anxiety disorder), MR (Mentally retarded), OCD (Obsessive compulsive disorder), PD (Parkinson's disease), PTSD (Post-traumatic stress disorder)

Table 3 - Crude prevalence of disorders among the population studied (principal diagnosis)

Disorders	Observed Cases (n)	Crude Prevalence Rate (%)	Crude Prevalence (%)	
			Female	Male
Schizophrenia	16,464	28.6	25.2	30.4
Depression	8096	14.0	20.0	10.8
Epilepsy	6576	11.4	13.0	10.5
GAD	4864	8.4	6.5	9.5
OCD	4352	7.5	6.5	8.1
Mood Disorder	3952	6.8	5.7	7.5
Mania	2912	5.0	4.2	5.5
BAD	2496	4.3	5.3	3.8
Psychosis	2224	3.9	4.8	3.3
Dementia	1456	2.5	2.5	2.5
DDD	880	1.5	0.2	2.3
Phobia	880	1.5	1.3	1.6
Insomnia	704	1.2	1.2	1.2
Cluster Headache	480	0.8	1.0	0.8
AD	224	0.4	0.5	0.3
Migraine	224	0.4	0.8	0.2
BDD	208	0.4	0.3	0.4
Cerebral Atrophy	208	0.4	0.3	0.4
PD	208	0.4	0.2	0.5
MR	80	0.1	0.3	0.0
CAPD	48	0.1	0.1	0.1
Hypomania	32	0.1	-	0.1
Cerebral Palsy	16	0.0	0.1	-
Paranoia	16	0.0	-	0.0
Parkinsonism	16	0.0	-	0.0
Postpartum Depression	16	0.0	0.1	0.0
PTSD	16	0.0	0.1	-
ADHD	16	0.0	-	0.0

NB: ADHD (Attention deficit hyperactivity disorder), AD (Alzheimer's disease), BAD (Bipolar affective disorder), BDD (Body dysmorphic disorder), CAPD (Central auditory processing disorder), DDD (Drug dependence disorder), GAD (Generalized anxiety disorder), MR (Mentally retarded), OCD (Obsessive compulsive disorder), PD (Parkinson's disease), PTSD (Post-traumatic stress disorder). Diagnosis as recorded in patient's notes

Table 4 – Psychotropic medicines prescribed for neurological and/or psychiatric disorders in order if use by treatment category

Medicines Prescribed	Female		Male	
	N	%	N	%
Antipsychotics	**23856**	**33.28**	**47648**	**35.08**
Clozapine	8480	11.83	16640	12.25
Risperidone	6160	8.59	12160	8.95
Olanzapine	5168	7.21	10864	8
Haloperidol	2544	3.55	5504	4.05
Quetiapine	960	1.34	1536	1.13
Fluphenazine	272	0.38	592	0.44
Levosulpiride	208	0.29	112	0.08
Zuclopenthixol	32	0.04	160	0.12
Trifluoperazine	16	0.02	32	0.02
Ziprasidone	16	0.02	32	0.02
Flupirtine	0	0	16	0.01
Antidepressants	**21200**	**29.57**	**39440**	**29.04**
Venlafaxine	6816	9.51	13520	9.96
Mirtazapine	6352	8.86	12832	9.45
Escitalopram	2752	3.84	4704	3.46
Fluoxetine	1936	2.7	2784	2.05
Fluvoxamine	1568	2.19	3232	2.38
Nortriptyline	1088	1.52	1440	1.06
Clomipramine	240	0.33	528	0.39
Citalopram	192	0.27	208	0.15
Paroxetine	144	0.2	112	0.08
Tianeptine	64	0.09	80	0.06
Sertraline	32	0.04	0	0
Duloxetine	16	0.02	0	0
Antiepileptics	**10256**	**14.31**	**18000**	**13.25**
Sodium Valproate	6064	8.46	10896	8.02
Carbamazepine	3296	4.60	5776	4.25
Divalproex Sodium	368	0.51	576	0.42
Topiramate	272	0.38	576	0.42
Levetiracetam	256	0.36	176	0.13
Anxiolytics and hypnotics	**9152**	**12.77**	**16176**	**11.91**
Clonazepam	3136	4.38	6848	5.04
Lorazepam	2352	3.28	2976	2.19
Alprazolam	2016	2.81	2944	2.17
Bromazepam	1488	2.08	3296	2.43
Medazepam	144	0.20	96	0.07
Oxazepam	16	0.02	16	0.01
Anti-Parkinson	**4352**	**6.07**	**7728**	**5.69**
Procyclidine	4352	6.07	7712	5.68

Levodopa/Carbidopa	0	0.00	16	0.01
Antihistamines	**2288**	**3.19**	**5696**	**4.19**
Promethazine	2272	3.17	5664	4.17
Chlorpheniramine	16	0.02	32	0.02
Miscellaneous	**576**	**0.80**	**1120**	**0.82**
Rivastigmine	544	0.76	1040	0.77
Memantine	32	0.04	48	0.04
Trimetazidine	0	0.00	16	0.01
Clofazimine	0	0.00	16	0.01
Total number Prescribed	**71680**	**100.0**	**135808**	**100.0**

Table 5 – Most frequently prescribed medicines according to sex

	Male			**Female**		
	Drug	**n=23424**	**%**	**Drug**	**n=10032**	**%**
Schizophrenia	Clozapine	5216	22.27	Clozapine	2224	22.17
	Venlafaxine	4768	20.36	Venlafaxine	1904	18.98
	Mirtazapine	4464	19.06	Mirtazapine	1968	19.62
	Risperidone	3536	15.10	Risperidone	1632	16.27
	Olanzapine	3312	14.14	Sodium Valproate	1328	13.24
	Promethazine	2128	9.08	Olanzapine	976	9.73
	Drug	**n=7984**	**%**	**Total**	**n=6970**	**%**
Depression	Clozapine	1792	44.44	Clozapine	1863	45.85
	Mirtazapine	1488	36.90	Mirtazapine	1638	40.31
	Risperidone	1456	36.11	Venlafaxine	1124	27.66
	Venlafaxine	1328	32.93	Risperidone	915	22.52
	Olanzapine	1008	25.00	Escitalopram	723	17.78
	Sodium Valproate	912	22.61	Alprazolam	707	17.39
	Drug	**n=5168**	**%**	**Total**	**n=6233**	**%**
Epilepsy	Sodium Valproate	1127	42.44	Sodium Valproate	1818	46.38
	Clozapine	1127	42.44	Clozapine	1488	37.95
	Mirtazapine	926	34.88	Carbamazepine	826	21.08
	Venlafaxine	926	34.88	Clonazepam	708	18.07
	Risperidone	542	20.40	Risperidone	708	18.07
	Carbamazepine	520	19.59	Mirtazapine	685	17.47

Table 6 – Neurological and psychological disorders among smokers, alcohol and drug misusers

Disorder	Smokers % (N=15264)		Alcohol misuse % (N=2896)		Drug misuse % (N=7200)	
	Female (N=272)	Male (N=14992)	Female (N=16)	Male (N=2880)	Female (N=48)	Male (N=7152)
AD	-	0.32	-	-	-	0.67
BAD	17.65	4.16	-	1.11	-	2.01
BDD	-	0.43	-	-	-	0.22
Cerebral Atrophy	-	0.43	-	-	-	0.67
Cluster Headache	-	0.85	-	0.56	-	0.89
Dementia	5.88	2.88	-	2.78	-	3.36
Depression	11.76	12.91	100	8.89	33.33	13.65
DDD	-	3.09	-	3.89	-	5.37
Epilepsy	-	7.90	-	6.67	-	7.61
GAD	-	9.39	-	9.44	-	9.40
Hypomania	-	0.11	-	-	-	0.22
Insomnia	5.88	1.07	-	1.11	-	1.12
Mania	-	4.70	-	6.67	-	4.47
Migraine	5.88	-	-	-	-	-
Mood Disorder	5.88	8.00	-	8.89	-	7.38
OCD	5.88	8.00	-	7.22	-	7.16
Paranoia	-	0.11	-	-	-	-
PD	-	0.64	-	0.56	-	3
Phobia	5.88	1.07	-	2.22	-	3
Psychosis	11.76	3.31	-	4.44	33.33	14
Schizophrenia	23.53	30.63	-	35.56	33.33	140

NB: AD (Alzheimer's disease), BAD (Bipolar affective disorder), BDD (Body dysmorphic disorder), DDD (Drug dependence disorder), GAD (Generalized anxiety disorder), OCD (Obsessive compulsive disorder), PD (Parkinson's disease)

Table 7 – Family history

Disorder (N)	Distribution of disorders		
Female (n=1808)			
	Parents	**Children**	**Sibling**
BAD (208)	16 (Cancer) 16 (MR) 16 (Schizophrenia)	16 (BAD) 16 (MR)	16 (BAD) 16 (Depression)
CAPD (16)	-	-	-
Cerebral Palsy (16)	-	-	16 (Cerebral Palsy)
Dementia (16)	16 (BAD)	-	-
Depression (528)	64(Depression) 32 (Epilepsy) 16 (Schizophrenia) 16 (AD)	96 (Epilepsy) 64 (Schizophrenia) 16 (Depression)	80 (MR) 64 (Depression) 16 (ADHD)
Epilepsy (336)	32 (Depression) 16 (Epilepsy)	32 (Epilepsy)	128(Epilepsy) 16 (Behavioural disorder) 16 (BAD)
GAD (16)	-	16 (Depression)	-
Mania (80)	16 (BAD)	-	16 (BAD) 16 (Depression) 16 (MR) 16 (Epilepsy)
MR (16)	-	-	16(MR)
Migraine (32)	-	-	32 (MR)
OCD (16)	16 (OCD)	-	-
Psychosis (96)	16 (Mania) 16 (Psychosis)	-	-
Schizophrenia (432)	96 (Schizophrenia) 32 (MR) 16 (Stroke)	16 (Depression) 16 (Schizophrenia)	64 (Schizophrenia) 32 (MR) 16 (Drug misusers) 16 (Epilepsy)
Male (n=1952)			
BAD (336)	5 (BAD) 1 (HCV) 1 (Depression)	-	112 (BAD) 32 (Schizophrenia) 16 (Epilepsy) 16 (Depression)
BDD (16)	16 (Drug misusers)	-	-
CAPD (16)	-	-	16 (CAPD)
Dementia (16)	-	-	16 (Schizophrenia)
Depression (112)	16 (BAD) 16 (Depression)	-	32 (Epilepsy) 16 (Behavioural disorder) 16 (Speech disorder) 16 (MR)
DDD (16)	-	-	-
Epilepsy (608)	32(Epilepsy) 16 (Depression) 16 (MR) 16 (BAD)	48 (Epilepsy) 16 (MR)	160 (Epilepsy) 16 (Sleep walking)
GAD (16)	16 (Drug misusers)	-	-
Mania (16)	16 (BAD)	-	16 (BAD)
MR (16)	-	-	16 (MR)
Migraine (16)	-	-	16 (MR)

Mood Disorder (16)	16(Drug misusers)	-	-
Psychosis (128)	16 (MR) 16 (BAD) 16 (Depression)		16 (Epilepsy) 16 (Psychosis) 16 (BAD)
Schizophrenia (624)	96 (Schizophrenia) 16 (BAD) 16 (Epilepsy) 16 (Depression) 16 (MR)	16 (Epilepsy & MR)	144 (Schizophrenia) 16 (Mood disorder) 16 (Psychosis) 16 (Disabled) 16 (Epilepsy) 16 (Speech problem)

NB: ADHD (Attention deficit hyperactivity disorder), AD (Alzheimer's disease), BAD (Bipolar affective disorder), BDD (Body dysmorphic disorder), CAPD (Central auditory processing disorder), DDD (Drug dependence disorder), GAD (Generalized anxiety disorder), MR (Mentally retarded), OCD (Obsessive compulsive disorder), PD (Parkinson's disease), PTSD (Post-traumatic stress disorder). ADHD was often found in multiple siblings

Appendix

Table A1 - Disorder ratio broken down by age

Age bands (Years)	Female Disorders	N	%age	Male Disorders	N	%age
0-19	Epilepsy	560	2.75	Schizophrenia	1504	4.03
	Schizophrenia	560	2.75	Epilepsy	704	1.89
	Depression	240	1.18	GAD	480	1.29
	Psychosis	160	0.79	Mania	480	1.29
	GAD	160	0.79	OCD	480	1.29
	Mania	144	0.71	Depression	448	1.20
	Mood Disorder	112	0.55	Mood Disorder	416	1.12
	OCD	112	0.55	Dementia	208	0.56
	BAD	64	0.31	Psychosis	176	0.47
	Migraine	48	0.24	Phobia	128	0.34
	MR	32	0.16	DDD	96	0.26
	CAPD	16	0.08	BAD	80	0.21
	Cerebral Palsy	16	0.08	Insomnia	80	0.21
	Cerebral Atrophy	16	0.08	AD	32	0.09
	AD	16	0.08	Cluster Headache	32	0.09
	-	-	0.00	ADHD	16	0.04
	-	-	0.00	CAPD	16	0.04
	-	-	0.00	Cerebral Atrophy	16	0.04
	-	-	0.00	Migraine	16	0.04
	-	-	0.00	PD	16	0.04
	-	-	0.00	BDD	16	0.04
20-29	Schizophrenia	1568	7.70	Schizophrenia	4176	11.20
	Depression	976	4.79	Epilepsy	1776	4.76
	Epilepsy	976	4.79	Depression	1632	4.38

	OCD	432	2.12	GAD	1152	3.09
	Mood Disorder	352	1.73	OCD	1104	2.96
	BAD	304	1.49	Mood Disorder	1008	2.70
	GAD	304	1.49	Mania	720	1.93
	Psychosis	240	1.18	BAD	368	0.99
	Mania	208	1.02	DDD	368	0.99
	Phobia	112	0.55	Psychosis	304	0.82
	Dementia	96	0.47	Dementia	256	0.69
	Cluster Headache	80	0.39	Phobia	240	0.64
	Insomnia	80	0.39	Insomnia	192	0.51
	AD	16	0.08	Cluster Headache	80	0.21
	MR	16	0.08	Cerebral Atrophy	64	0.17
	PD	16	0.08	PD	64	0.17
	-	-	0.00	BDD	48	0.13
	-	-	0.00	Migraine	48	0.13
	-	-	0.00	AD	32	0.09
	-	-	0.00	Hypomania	32	0.09
	-	-	0.00	MR	16	0.04
	-	-	0.00	Paranoia	16	0.04
30-39	Schizophrenia	1472	7.23	Schizophrenia	3152	8.45
	Depression	960	4.71	GAD	1120	3.00
	Epilepsy	640	3.14	Depression	896	2.40
	GAD	416	2.04	Mood Disorder	832	2.23
	Mood Disorder	416	2.04	Epilepsy	784	2.10
	OCD	368	1.81	OCD	768	2.06
	Psychosis	304	1.49	Psychosis	512	1.37
	BAD	288	1.41	Mania	448	1.20
	Mania	224	1.10	BAD	384	1.03
	Dementia	128	0.63	Dementia	272	0.73

	Insomnia	112	0.55	DDD	224	0.60
	Phobia	80	0.39	Insomnia	128	0.34
	BDD	64	0.31	Phobia	128	0.34
	Cluster Headache	64	0.31	Cluster Headache	64	0.17
	AD	48	0.24	BDD	48	0.13
	Migraine	48	0.24	PD	48	0.13
	DDD	32	0.16	AD	32	0.09
	Cerebral Atrophy	16	0.08	CAPD	16	0.04
	Postpartum Depression	16	0.08	Cerebral Atrophy	16	0.04
	PTSD	16	0.08	Migraine	16	0.04
40-49	Depression	832	4.08	Schizophrenia	1648	4.42
	Schizophrenia	576	2.83	GAD	544	1.46
	BAD	240	1.18	Depression	528	1.42
	Epilepsy	208	1.02	OCD	512	1.37
	GAD	160	0.79	Epilepsy	480	1.29
	Mania	128	0.63	Mood Disorder	352	0.94
	OCD	128	0.63	BAD	336	0.90
	Psychosis	112	0.55	Mania	272	0.73
	Dementia	96	0.47	Psychosis	160	0.43
	Mood Disorder	96	0.47	Dementia	128	0.34
	Migraine	32	0.16	DDD	112	0.30
	Cerebral Atrophy	16	0.08	Cluster Headache	96	0.26
	Cluster Headache	16	0.08	Phobia	96	0.26
	Insomnia	16	0.08	Insomnia	48	0.13
	MR	16	0.08	Cerebral Atrophy	32	0.09
	Phobia	16	0.08	PD	32	0.09
	-	-	0.00	BDD	16	0.04
50-59	Depression	528	2.59	Schizophrenia	528	1.42
	Schizophrenia	448	2.20	Depression	272	0.73

	Epilepsy	176	0.86	BAD	128	0.34
	OCD	176	0.86	Epilepsy	128	0.34
	GAD	144	0.71	GAD	96	0.26
	BAD	128	0.63	Mood Disorder	80	0.21
	Mood Disorder	80	0.39	Mania	64	0.17
	Dementia	64	0.31	OCD	64	0.17
	Mania	64	0.31	Psychosis	64	0.17
	Phobia	48	0.24	BAD	32	0.09
	Psychosis	48	0.24	Dementia	32	0.09
	Cerebral Atrophy	16	0.08	AD	16	0.04
	Cluster Headache	16	0.08	Cerebral Atrophy	16	0.04
	Insomnia	16	0.08	Cluster Headache	16	0.04
	Migraine	16	0.08	DDD	16	0.04
	-	-	0.00	Insomnia	16	0.04
	-	-	0.00	PD	16	0.04
Above 60	Depression	528	2.59	Schizophrenia	320	0.86
	Schizophrenia	512	2.51	Depression	256	0.69
	GAD	144	0.71	GAD	144	0.39
	Dementia	128	0.63	Mood Disorder	96	0.26
	Mood Disorder	112	0.55	OCD	96	0.26
	OCD	112	0.55	BAD	80	0.21
	Psychosis	112	0.55	Mania	80	0.21
	Mania	96	0.47	Dementia	48	0.13
	Epilepsy	80	0.39	Epilepsy	48	0.13
	BAD	64	0.31	DDD	32	0.09
	AD	16	0.08	Psychosis	32	0.09
	Cluster Headache	16	0.08	AD	16	0.04
	Insomnia	16	0.08	BDD	16	0.04

	PD	16	0.08	Parkinsonism	16	0.04
	Phobia	16	0.08	Phobia	16	0.04

NB: CAPD (Central auditory processing disorder), DDD (Drug dependence disorder), MR (Mentally retarded), PD (Parkinson's disease), ADHD (Attention deficit hyperactivity disorder), AD (Alzheimer's disease), BAD (Bipolar affective disorder), BDD (Body dysmorphic disorder), GAD (Generalized anxiety disorder), OCD (Obsessive compulsive disorder), PTSD (Post-traumatic stress disorder)

Table A2 - Co-morbidities related to neurological and psychological disorders in both male and female populations

Disorder	**Co-Morbidities**	**No. of Cases**	**Disorder**	**Co-Morbidities**	**No. of Cases**
AD	HTN	16	AD	DM	16
BAD	Depression	32		HTN	16
	Hep-C	16	BAD	DM, Hep-C	32
	HTN	48		Hallucinations	16
	Polio	16		IHD	16
	Ulcer	16		Hep C	16
	UTI	16		HTN, DM	16
BDD	Diabetes	16		Insomnia	32
Cerebral atrophy	HTN	16		Paralysis	16
Cluster headache	HTN	32		Typhoid	16
Cerebral palsy	Speech Delay	16	BDD	DM	32
Dementia	Diabetes	80		HTN	48
	HTN	48	CAPD	Developmental delay	16
	Schizophrenia, HTN, DM	16	Cerebral atrophy	DM	16
Depression	Anxiety	32		HTN	32
	Anxiety & Insomnia	16	Cluster headaches	DM	64
	Asthma	16		HTN	80
	CA Breast	16	Dementia	DM	112
	Dengue	16		HTN	128
	DM	208	Depression	AIDS	16
	DM, HTN	32		Anxiety	16
	HTN	352		Behaviour Disorder, Insomnia	16
	Gall bladder Stones	16		HTN	256
	IHD	16		DM	480
	HTN, Insomnia	16		Seizures	32
	Insomnia	112		Hep-C	16
	Migraine	32		Insomnia	48
	Mood Disorder	16		Jaundice	16
	Partial paralysis	16	Epilepsy	Anemia	16
	Piles, Nephrolethiasis	16		Anxiety	32
	Stroke	16		Behavioural Disorder	32

	Typhoid	16		Blindness	16
	Ulcer/Severe Headache	16		DM	384
	Urolithiasis	16		Ear infection	16
Epilepsy	DM	112		Seizures	16
	Seizures	16		Head injury	32
	HTN	192		Herper zoster	16
	Mania	16		HTN	496
	Memory Loss	16		Jaundice	16
	Meningitis	16		Meningitis	32
	MR	16		Pneumonia	16
	Pneumonia	32		Polio	16
	Psychosis, typhoid	16		Psychosis	16
	Typhoid	48		Speech/language delay disorder	16
	Typhoid, Dengue	16		Typhoid	128
GAD	DM	240	GAD	DM	624
	HTN	112		HTN	400
	Insomnia	16		Memory loss	16
	Memory loss	32	Hypomania	HTN	16
	Renal disease, Hep-C	16	Insomnia	DM	80
Insomnia	DM	48		HTN	16
	HTN	16	Mania	DM	352
Mania	Anxiety	16		Head injury	16
	Arthritis	16		HTN	128
	Depression	16		Typhoid	16
	DM	80	MR	Developmental delay	16
	HTN	80	Mood disorder	DM	416
	Memory loss	32		HTN	336
	Brain Tumour	16		Memory loss	32
MR	Developmental delay	16	OCD	Anxiety	16
	DM	16		Asthma	16
	Meningitis	16		DM	512
Migraine	Anxiety	16		HTN	480
	Asthma, DM	16		Memory loss	16
Mood disorder	DM	160	Paranoia	Anxiety	16
	HTN	160	PD	DM	32
OCD	Anxiety	16		HTN	16
	DM	288	Phobia	DM	144
	HTN	224		HTN	48
PD	HTN	16	Psychosis	Anxiety	16
Phobia	DM	32		Dengue	16
	HTN	32		Depression	16
Psychosis	Angina	16		DM	80

	Anxiety	16		Epilepsy	16
	Depression	64		Hep-C	16
	DM	64		HTN	96
	HTN	80		TB	32
	Arthritis	16		Typhoid	32
	Learning disability	16	Schizophrenia	Angina	16
	Mania	16		Anxiety	112
	Migraine	16		Arthritis	16
	MR	16		BAD	16
	Typhoid	16		Dengue	16
Schizophrenia	Anorexia	16		DM	1648
	DM, HTN	16		Head injury	16
	DM, HTN, Paralysis	16		Hep-C, Depression	16
	IHD	32		HTN	1248
	Dengue	16		HTN, DM	32
	Depression	64		Hydrocephalus	16
	DM	544		Kidney stone	16
	Seizures	16		Mania	16
	Hep-C	16		Memory loss	32
	HTN	528		MR	16
	Jaundice	16		Mood disorder	16
	Memory loss	32		Phobia	16
	MR	32		Psychosis	16
	Mood disorder	16		Seizures	32
	Phobia	16		Typhoid	16

NB: AD (Alzheimer's disease), BAD (Bipolar affective disorder), BDD (Body dysmorphic disorder), DM (Diabetes mellitus), GAD (Generalized anxiety disorder), HTN (Hypertension), IHD (Ischemic heart disease), Hep-C (Hepatitis C), MR (Mentally retarded), OCD (Obsessive compulsive disorder), PD (Parkinson's disease), UTI (Urinary tract infection)